Citation:

Weijenberg MP, Mullie PF, Brants HA, Heinen MM, Goldbohm RA, van den Brandt PA. Dietary glycemic load, glycemic index and colorectal cancer risk: Results from the Netherlands Cohort Study. *Int J Cancer.* 2008 Feb 1; 122(3): 620-629.

PubMed ID: 17935129

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate whether a diet with a high glycemic load (GL) or glycemic index (GI) is associated with increased colorectal cancer risk.

Inclusion Criteria:

- The cohort consisted of 120,852 subjects (48% men and 52% women), aged 55 to 69 years at the beginning of the study, who completed a baseline questionnaire. This self-administered mailed questionnaire covered dietary habits, lifestyle, smoking, family history of cancer and demographic data
- The investigation was performed within the framework of the Netherlands Cohort Study on diet and cancer that started in September 1986.

Exclusion Criteria:

All prevalent cancer cases at baseline other than non-melanoma skin cancer.

Description of Study Protocol:

Recruitment

- The investigation was performed within the framework of the Netherlands Cohort Study on diet and cancer that started in September 1986
- The cohort consisted of 120,852 subjects (48% men and 52% women), aged 55 to 69 years at the beginning of the study, who completed a baseline questionnaire. This self-administered mailed questionnaire covered dietary habits, lifestyle, smoking, family history of cancer and demographic data.

Design

Prospective cohort study; case cohort approach.

Dietary Intake/Dietary Assessment Methodology

- The subjects completed a semi-quantitative FFQ that included 150 food items and covered habitual food habits during the year before the start of the study. They could indicate their frequency of consumption by choosing pre-defined frequency categories and the portion size per consumption frequency in natural or household units or grams, depending on the type of food
- The questionnaire was validated and tested for reproducibility. Nutrient intakes were calculated from each food on the questionnaire as the frequency of consumption multiplied by the number of units, the size of a unit and the nutrient content of the food, using a computerized Dutch food composition table
- Subjects with incomplete dietary data were excluded from the analyses (7.0%). Data were considered incomplete when 60 or more questionnaire items were blank and when fewer than 35 items at least were eaten once per month.

Blinding Used

The questionnaire data of all cases and subcohort members were processed in a manner blinded with respect to case/subcohort status to minimize observer bias in the coding and interpretation of data.

Statistical Analysis

- Glycemic load and GI were adjusted for energy intake using the residual method as described by Willett and Stampfer
- Body mass index [BMI = weight (kg)/height^2 (m^2)] was calculated from self-reported height and weight of the individuals. Pearson's product moment correlation coefficients between GL, GI and selected nutrient intakes were calculated. Because of the non-normal distribution of alcohol intake, Spearman's rank-order correlation coefficient was used. X^2 tests were conducted to test the difference in distribution of categorical variables according to quintiles of energy-adjusted GL and GI
- Because the etiology of colorectal cancers may vary according to sex and sub-site of the cancer, men and women were analyzed separately for colorectal, colon, proximal colon, distal colon and rectal cancers
- Cox proportional hazards analysis was used in the case cohort analyses to obtain hazard rate ratios (RRs) and 95% CIs for the association between GL, GI and the incidence of overall colorectal, colon, proximal colon, distal colon or rectal cancers.

Data Collection Summary:

Timing of Measurements

- Semiquantitative FFQ at baseline in 1986
- 11.3 years of follow-up.

Dependent Variables

Colorectal cancer risk.

Independent Variables

- Glycemic load
- Glycemic index.

Description of Actual Data Sample:

- *Initial N:* 120,852 subjects (48% men and 52% women)
- *Attrition (final N):* A total of 1,361 colon (736 men and 625 women) and 450 rectal (295 men and 155 women) cancer cases were detected in the cohort after 11.3 years of follow-up
- *Age:* 55 to 69 years
- *Ethnicity:* Dutch
- *Location:* Netherlands.

Summary of Results:

Key Findings

The RR for colorectal cancer comparing the highest vs. the lowest quintile levels of glycemic load and glycemic index were 0.83 (95% CI: 0.64 to 1.08) and 0.81 (95% CI: 0.61 to 1.08) for men and 1.00 (95% CI: 0.73 to 1.36) and 1.20 (95% CI: 0.85 to 1.67) for women.

Hazard Rate Ratios for Colorectal Cancers According to Quintiles of Energy-adjusted Glycemic Load and Glycemic Index in the Male Population of the Netherlands Cohort Study

Quintiles of Energy-adjusted Glycemic Load						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P for Trend**
Median glycemic load (g per day)	109.8	124.8	136.2	147.8	165.4	
Person-years in subcohort	4,188	4,245	4,147	4,255	4,203	
Colon-rectum						
No. cases	253	216	193	223	197	
RR[3] (95% CI)	1.00	0.82 (0.64 to 1.04)	0.75 (0.58 to 0.97)	0.90 (0.70 to 1.16)	0.83 (0.64 to 1.08)	0.37

RR[3] = Adjusted for age, BMI, family history of colon cancer, smoking, total energy intake, intake of calcium, intake of alcohol, educational level, intake of processed meat and physical activity.

Hazard Rate Ratios for Colorectal Cancers According to Quintiles of Energy-adjusted Glycemic Load and Glycemic Index in the Male Population of the Netherlands Cohort Study

Quintiles of Energy-adjusted Glycemic Index

	Q1	Q2	Q3	Q4	Q5	P for Trend
Median glycemic index	56.6	59.1	60.6	62.2	64.5	
Person-years in subcohort	4,263	4,160	4,099	4,212	4,305	
Colon-rectum						
No. cases	228	214	220	220	200	
RR[3] (95% CI)	1.00	0.93 (0.73 to 1.19)	1.00 (0.78 to 1.28)	0.98 (0.75 to 1.29)	0.81 (0.61 to 1.08)	0.27

Hazard Rate Ratios for Colorectal Cancers According to Quintiles of Energy-adjusted Glycemic Load and Glycemic Index in the Female Population of the Netherlands Cohort Study

Quintiles of Energy-adjusted Glycemic Load						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P for Trend**
Median glycemic load (g per day)	82.5	94.0	101.7	107.9	123.6	
Person-years in subcohort	4,423	4,490	4,510	4,352	4,200	
Colon-rectum						
No. cases	152	149	156	156	142	
RR[3] (95% CI)	1.00	0.96 (0.73 to 1.28)	1.02 (0.77 to 1.37)	1.05 (0.78 to 1.41)	1.00 (0.73 to 1.36)	0.81

Hazard Rate Ratios for Colorectal Cancers According to Quintiles of Energy-adjusted Glycemic Load and Glycemic Index in the Female Population of the Netherlands Cohort Study

Quintiles of Energy-adjusted Glycemic Index						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P for Trend**
Meridian glycemic index	53.7	56.2	57.8	59.6	61.9	
Person-years in subcohort	4,364	4,472	4,439	4,450	4,250	
Colon-rectum						
No. cases	132	159	173	144	147	

RR[3] (95% CI)	1.00	1.18 (0.89 to 1.56)	1.32 (0.98 to 1.76)	1.08 (0.80 to 1.47)	1.20 (0.85 to 1.67)	0.52

Other Findings

Glycemic load and glycemic index were borderline significantly associated with an increased risk of proximal colon cancer in women (P=0.06 and 0.08, respectively); however, these associations were attenuated after exclusion of the first two years of follow-up (P=0.165 and 0.254, respectively). In men, glycemic index was associated with a reduced risk of distal colon cancer (P=0.03).

Author Conclusion:

A diet with a high GL or GI was not associated with a higher risk of colorectal cancer in men or women.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	N/A
3.	**Were study groups comparable?**	No
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	No
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
	8.6.	Was clinical significance as well as statistical significance reported?	N/A
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes